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Epilepsy and Ramadan

The worldwide prevalence of epilepsy is over 65 million with greater prevalence in low income countries where access to diagnosis and management of epilepsy are also limited¹. Prevalence in the UK is approximately 600,000². Specific prevalence of epilepsy amongst the global Muslim population of 1.6 billion³, 3.4 million in the UK⁴, is not known though the disease burden is likely significant given the high prevalence in lower income countries where much of this population reside. Amongst Western Muslim populations factors such as inadequate or delayed access to medical services for lower socioeconomic groups; stigma surrounding epilepsy; consanguinity increasing genetic risk; presentation of symptomatic causes of epilepsy amongst immigrants not often encountered in Western populations; and a reliance on alternative or complementary therapies as well as conventional medicines may all contribute to challenges in the management of epilepsy⁵.

Ramadan, the ninth month of the Islamic calendar, obliges adult Muslims to refrain from eating, drinking and conjugal relations from dawn until sunset for up to 30 days consecutively. Muslims are accustomed to a dramatic change of routine in this month involving an early pre-dawn meal (suhoor), a late post-sunset meal (iftar) and daily late-night prayers at the mosque or at home. The Islamic calendar is based on the lunar cycle meaning months cycle through the seasons, shifting by 11 days annually in relation to the Gregorian calendar. The length of the day and hence the fast in countries further from the equator such as the UK can be up to 20 hours in Summer. In 2020 Ramadan will begin in late April and end in late May; with fasts in the UK expected to be approximately 17-18 hours long. Rather than being perturbed by these challenges, many Muslims see Ramadan as a time of heightened spiritual fervour and community cohesion. Indeed fasting in Ramadan is more likely to be observed globally (93%)⁶ and by Western Muslims (80% in USA)⁷ than other obligations such as the five daily prayers.

Fasting in Ramadan presents a specific challenge for patients with epilepsy. Studies by Gomceli et al⁸ and Abdou et al⁹ have demonstrated an increase in incidence of seizures amongst known epileptics during Ramadan. Advice and recommendations for fasting patients and their health care providers in a number of chronic health conditions¹⁰, particularly diabetes¹¹, are now available aiding informed decision making. Advice specific to epilepsy is not readily available. This article aims to detail some of the relevant issues to facilitate health care professionals working with patients with epilepsy who are participating in Ramadhan; and also highlighting for Muslims with epilepsy the available options both in terms of religious law and management of epilepsy.

Seizure risk during Ramadan

Various factors can contribute to increased seizure risk in Ramadan.

Changes to drug regimens are commonly required and may or may not be led by the physician. Driven by their zeal to participate in the religious customs, many Muslims with epilepsy may take risks particularly with altering drug regimens¹². Most often this is due to the usual dosing regimen being incompatible with the length of fasts, particularly with twice daily dosing in Summer months when all oral consumption is condensed into a short period at night. Alteration to drug regimens in Ramadan is linked to a higher risk of increased seizure frequency than fasting with unaltered drug regimens^{8,9}. Moreover, Muslim patients may hesitate to seek or dismiss the opinion of their health care professionals due to an assumption that religious needs and considerations won't be understood or validated¹³. Physicians also may feel ill equipped to provide culturally sensitive advice and may inadvertently rely on preconceptions of the patient's views rather than exploring the reasons for poor adherence to medication¹³.

Participation in Ramadan can involve a significant change to routines and sleep patterns, fasting Muslims will often sleep and awaken later and will awaken through the night for a pre-dawn meal before the fast commences. Working hours are often adjusted to account for this in Muslim majority countries but this can present an added challenge for Muslims in non-Muslim majority countries. Disruption of sleep patterns and fatigue are frequently reported seizure triggers¹⁴ and sleep structure is known to be altered during periods of fasting with delayed sleep onset and impaired REM sleep¹⁵. This effect however has not been found in daytime sleepiness, cognitive function, sleep architecture, and circadian rhythm when lifestyle changes in Ramadan are controlled for, suggesting there is no inherent effect of fasting on these factors¹⁶. Adequate advice around obtaining enough sleep or adjusting sleeping patterns to incorporate daytime sleep should be provided.

Dehydration and hypoglycaemia may be concerns in periods of hot weather or long fasts. Particular attention may need to be given to patients taking Topiramate due to compounded risk of nephrolithiasis.

Identifying at risk patients

In preparation for Ramadan, it is vital that patients and their doctors are able to form a plan for managing their seizure disorder and anti-epileptic drug (AED) use. We have suggested a stratification of patients into high or low risk depending on the tendency towards experiencing severe or prolonged seizures. In general, safe fasting is usually possible for most people with epilepsy if they follow medical advice. Figure 1 below provides general guidance on risk stratifying patients and advice on fasting status, patients should be considered on a case by case basis. We envisage that people with epilepsy hoping to fast in Ramadan would consult with their treating physician or epilepsy specialist nurse at least 3 months prior to the commencement of Ramadan.

Minimal risk	High risk
<ul style="list-style-type: none"> •Normal MRI •Normal EEG •1-2 Seizures whole adult life •Maintained on single monotherapy because of low seizure burden •Moderate dose 	<ul style="list-style-type: none"> •Abnormal MRI •Abnormal EEG •Frequent Seizures •Maintained on combination AED because of poorly controlled seizures in past •Previous Status Epilepticus •Co-morbid conditions like BP, heart failure, malignancy, diabetes •Elderly

Figure 1 - Risk stratification of patients with epilepsy and suitability of fasting in Ramadan

Drugs

Attributes of certain antiepileptic drugs (AEDs) such as half-life, side effects and method of clearance will affect their suitability for use in patients fasting during Ramadan. These considerations should be made in light of the time of year – fasts in Summer can be up to 20 hours long whilst in Winter may only be 9-10 hours long.

Drug name	Typical maintenance dose	Half-life (hr)	Method of clearance
Lamotrigine	75-200mg BD	10-30	Hepatic
Levetiracetam	1500mg BD	<10	Renal
Sodium valproate	60mg/kg/day, BD/TDS if IR, OD if MR	10-30	Hepatic
Carbamazepine	Up to 2.4g/day, TDS if IR, BD if MR	10-30	Hepatic
Phenytoin	200-500mg, OD or 2 divided doses	10-30	Hepatic
Lacosamide	100-200mg BD	10-30	Renal
Perampanel*	4-12mg OD	>30	Hepatic
Topiramate	125-200mg in 2 divided doses	10-30	Hepatic + renal
Zonisamide*	400-600mg OD	>30	Renal
Clobazam	20mg in 2 divided doses	10-30	Hepatic
Clonazepam*	Up to 4-8mg OD if stable dose	30-40	Hepatic
Pregabalin	200-600mg in 2-3 divided doses	<10	Renal

Table 1 - AED attributes to consider in Ramadan prescribing.

* = potentially suitable for once daily dosing.

OD = once daily. BD = twice daily. IR = immediate release. MR = modified release

Adapted from 'Choosing antiepileptic drugs' Doyle, Alick 2018¹⁷

Table 1 highlights attributes of AEDs which can aid in decision making around prescribing in Ramadan. Commonly prescribed AEDs such as Lamotrigine, Levetiracetam and Carbamazepine require twice daily dosing, and this can be difficult to implement in Summer months when the length of the fast is long and oral consumption is condensed into a short period overnight. It may be possible to take doses at the post-sunset and pre-dawn meals, thereby shortening the period in between doses compared to the usual routine but maintaining twice daily dosing. The minimum acceptable time period in between doses will vary depending on the drug, side effect profile and nature of seizure disorder but doses less than 6 hours apart may not be advisable. Drugs such as Perampanel, Zonisamide and Clonazepam which can be given once daily may be more suitable in these patients. It may be possible to prescribe AEDs conventionally given as a split dose twice daily, such as Lamotrigine or Levetiracetam, in one larger dose once daily. Again, this is dependent upon factors such as side effects and nature of seizures. Patients receiving renally excreted drugs such as Levetiracetam, Lacosamide, Zonisamide and Topiramate should be counselled about the added risks of dehydration, particularly of the increased risk of nephrolithiasis with Topiramate.

Islamic rulings regarding Ramadhan and exemptions from fasting

At its foundation Islamic law, the Shari'ah, aims to protect core values including an individual's life, wellbeing and wealth. A degree of difficulty as a means of encouraging virtues such as patience is expected in Ramadan for those partaking in it, however religious law encourages the pre-emption of potential harm to health and wellbeing and provides exemptions and alternatives in place of the usual rituals. Islamic rulings make several exceptions to lift the obligation for fasting for those in whom it may entail hardship such as the elderly, those who are travelling, pregnant women and those with significant mental health illness. Those with pre-existing or current physical illness which may be significantly exacerbated by fasting are permitted to not fast. Such judgements may be based on previous experience of illness or the opinion of a qualified physician as well as a knowledgeable religious authority. If an individual is deemed high risk for fasting on medical grounds as per the criteria laid out in figure 1, this would confer a sufficient risk to their health in the opinion of religious law to consider them exempt from the obligation to fast and consider one of the alternatives below. It should be noted however that seizure disorders which present no threat to

quality of life such as minor seizures with no loss of consciousness would not be considered a sufficient threat to life or wellbeing.

Consideration should also be given to the potential impact of seizures or medication changes on driving status; breakthrough seizures or medication substitutions/reductions would necessitate not driving for 12 months and 6 months respectively for patients with group 1 licenses¹⁸. Subsequent impact on patient's ability to continue employment or on public safety should be carefully considered when judging an individual's suitability for fasting.

Those exempted from fasting at a particular timepoint have several options dependent on their circumstances: 1) if the reason for exemption is temporary such as an acute monophasic illness, fasts can be made up at a later date once the person has recovered; 2) if the length of the fast is the causative issue and shorter fasts are feasible then fasts can be made up at another time of year; 3) if the barrier to fasting is expected to be insurmountable in the future then charitable donations of a specific amount to feed the poor, termed 'fidyah', can take the place of fasting.

Although some routes of administration of medicines may be permitted during the fast by Islamic scholars, all agree that oral consumption of medicines is not allowed during the fast.

It should be recognised that although unanimous opinion exists on certain issues, there is a breadth of opinion on a variety of issues and health-care providers may encounter Muslims with differing viewpoints on these issues. Furthermore, Muslim patients may not have an in-depth knowledge of some of the concepts discussed above. A layperson's level of familiarity may be present, both of the medical and religious issues at hand.

Decision making in the clinic

Figure 2 proposes a flow chart that can be used as a decision-making aid bringing together the issues discussed thus far to demonstrate potential approaches to patients in the clinic. Factors considered are the inherent seizure risk of the patient; the length of the fast dependent on the time of year; and the patient's dosing regimen. Other factors to consider include occupation, driving status, risk of dehydration and sleep patterns.

The benefits of shared decision making in the epilepsy clinic are known¹⁹ and are especially applicable in this case. Exploring factors such as the importance of fasting to the individual; personal challenges around employment and sleep; concerns around medication changes and side effects; and the impact of any breakthrough seizures should all be considered. The potential for patients to dismiss medical advice particularly if it is seen to be rigid and uncompromising should not be ignored. Education regarding the risks of poor compliance with medication and increased seizure risk during Ramadan may be important in helping the patient make a balanced and informed decision on whether to fast. Low to moderate risk patients who are aware of the risks can be supported in their decision to fast with the necessary medical and practical precautions in place. Conversely high-risk patients who are determined to fast can be directed to seek further guidance from reliable religious sources and the exemption from fasting to protect life and wellbeing in Islamic law can be emphasised.

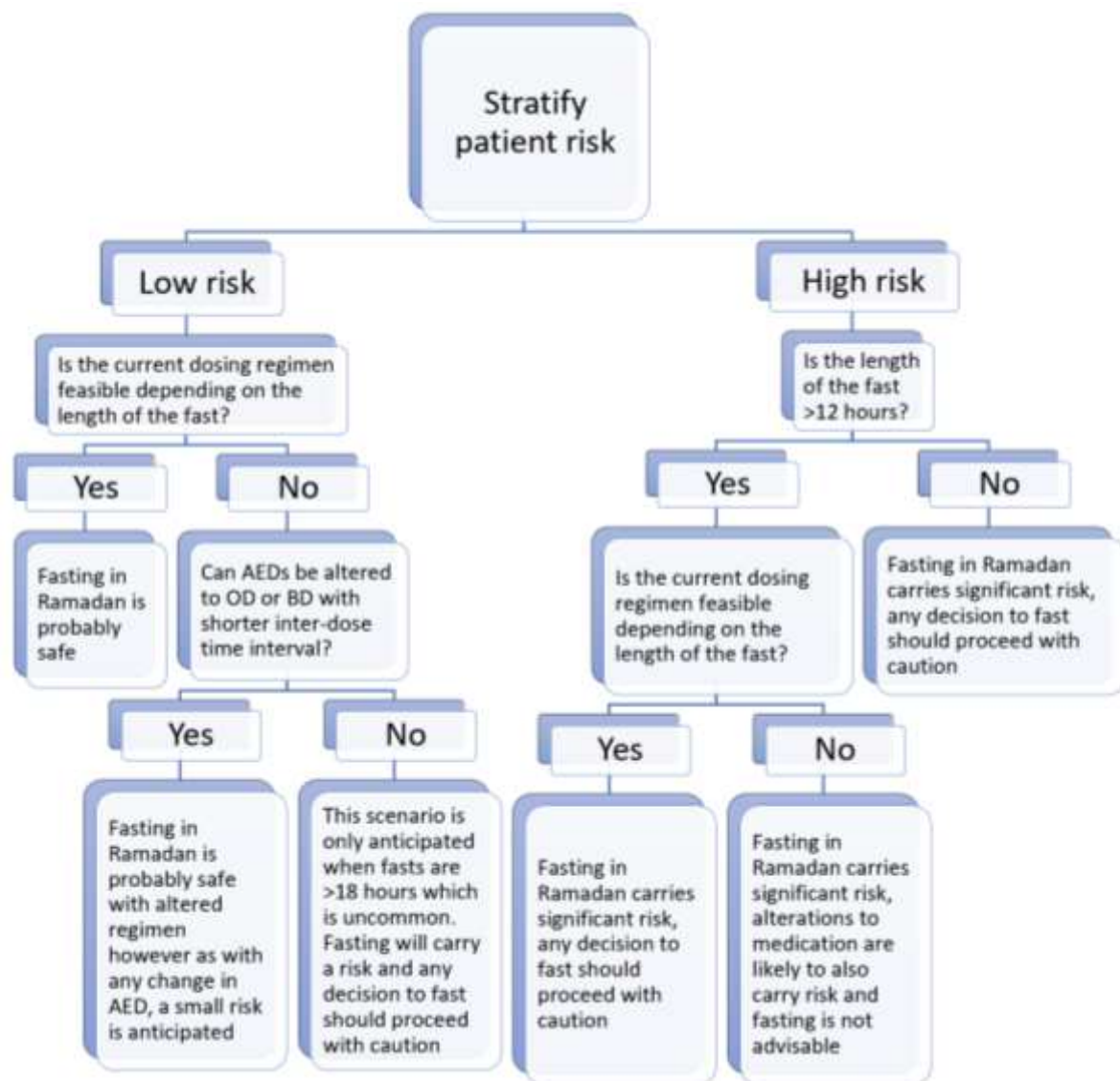


Figure 2 - Decision making aid

Conclusion

Epilepsy is common worldwide and a large number of Muslims with epilepsy will choose to fast during the month of Ramadan. Advice specific to epilepsy and fasting for health care professionals and patients is scarce. Seizure risk is increased during periods of fasting and usual medication regimens often require alteration during Ramadan. We have proposed stratifying patients into low and high risk based on nature of epilepsy and likelihood of seizure recurrence. Islamic law allows for exemption from fasting in cases where there is significant threat to an individual's life and wellbeing and alternatives to the usual rituals are highlighted. Alteration of drug regimens when safe may be required, either switching to OD dosing or maintaining BD dosing with shortened gap between doses. Shared decision making with weight given to both the patient's medical needs and religious preferences is encouraged. Further education amongst healthcare professionals as well as Muslim patients regarding both the risks of fasting in epilepsy and the alternative approaches offered by Islamic rulings is required.

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